

CHOLERA

War Department, Washington 25, D. C. . . . February 1945

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This bulletin follows TB MED 137, subject, "Physical Reconditioning for Bed and Ward Ambulant Patients." Distribution given TB MED 137 was as follows: AGF (5); ASF (2); T of Opns (25); S Div ASF (1); Dept (5); Base Comd (5); Ia Comd (5); Arm & Sv Bd (2); Def Comd (5); Tech Sv (2); SvO (10); Named & Numbered GH (60); Numbered GH (NP) CZ (45); Named SH (Including RH & Numbered SH) (40) except AAF (0); M Cono C (55); Gen Disp (ZI) (10); Fld Hosp (15); Hosp Tn (2); Hosp Ship Plat (5); Hosp Ship Complements (15); Conv. Ctr (15); Conv. Camp (10); Vet Gen Hosp (10); Vet Sta Hosp (10); Vet Evac Hosp (5); Vet Conv Hosp (5); Portable Surg Hosp (5); Evac Hosp (750 bed) (40); Evac Hosp (SH-400 bed) (30); Conv Hosp (20) except AAF (0); Gen & Sp Sv Sch (5); Enlisted Techn Sch 8 (1); USMA (2); ASTPU (3); ROTC (2); Army Med Tng C (60); Ind Sta (10); Sv C Lab (5); A (5); CHQ (5); D (55); AF (55); One copy to each of the following: T/O & E 3-25; 4-45; 4-145; 4-232; 5-35; 5-72; 5-95; 5-275; 6-35; 6-55; 6-65; 6-75; 6-95; 6-175; 6-325; 6-355; 6-365; 6-395; 7-85; 9-12; 11-25; 17-55; 17-125; 18-25; 19-35; 20-42. Two copies to each of the following: T/O & E 2-22; 4-152; 4-260-1; 5-386; 5-535S; 6-12; 6-45; 8-22; 8-26; 8-520; 9-35; 9-76; 10-22; 10-165; 10-217; 11-15; 17-15; 18-10-1; 18-35; 19-55; 20-46; 44-15; 44-25; 44-75; 44-115; 44-125; 44-225S; 44-315; 55-120-1. Three copies to each of the following: T/O & E 5-192; 7-95; 8-27; 10-45; 10-175; 17-115; 44-135; 44-320; 55-110-1; T/O & E 5-21 (5); 5-251 (6); 5-510S (35); 8-28 (10); 8-510 (15); 8-534 (5); 8-537T (15); 8-550 (60); 8-550S (45); 8-560 (40); 8-572S (5); 8-580 (40); 8-581 (30); 8-590 (20); 8-591T (15); 8-595T (10); 8-650 (10); 8-750 (10); 8-760 (10); 8-780 (5); 8-790 (5); 10-95 (7); 10-125 (6).

General	Paragraph	Diagnosis	Paragraph
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1. GENERAL. Cholera is an acute enteric infection in which the *Vibrio comma* is the specific etiologic agent. Although the organism may persist in nature under favorable circumstances for at least a few days, infection is usually traceable to patients in the immediate neighborhood. Patients in the incubation stage and those with mild symptoms or subclinical infections are important potential sources. Convalescent patients may remain carriers of virulent organisms for a short period of time. Recent studies have cast doubt upon the existence of true carriers. Susceptible individuals acquire the disease through the ingestion of food, drink, or other material contaminated by feces which contain the specific organism. Attacks of

cholera in an exposed group of individuals often appear to be distributed capriciously, probably because of the occurrence of subclinical attacks in the community. It is widely believed that any preexisting intestinal disturbance predisposes to the disease. Contamination of water is one of the most important means of spreading cholera. Flies may play an important role. Epidemics are seasonal, since their development is favored by climatic conditions, such as high temperature, high relative humidity, and intermittent heavy rainfall. In some areas, epidemics are associated with floods. Once a cholera epidemic gets under way, unless effective control is exercised, it rapidly sweeps

through an unprotected population and spreads along lines of communication with a speed proportional to that of the available means of transportation.

2. GEOGRAPHIC DISTRIBUTION. The best known endemic center of cholera is in the region of the lower Ganges River in Bengal, eastern India. The disease is said to be always present in this area. Other endemic areas may exist in Burma, southern China, and elsewhere, but their continuous existence is uncertain. Cholera often spreads throughout India and Burma. In recent years relatively few cases have appeared in Ceylon or to the west of India. During the summer in many years, cholera spreads extensively to the eastward. For some years before the war, British Malaya and the Netherlands East Indies (except for a small, somewhat questionable, epidemic in Celebes in 1937-39) were practically free of the disease. The same was true of the Philippines, except for the years 1930-34. Cholera often appears in Thailand, French Indo-China, Hong Kong, and Canton. It spreads northward through the ports of the China coast (such as Swatow, Amoy, Foochow, Wenchow, Shanghai, Tsingtao, and Tientsin). From these ports, the disease invades neighboring inland areas, especially the valley of the Yangtse River through which it reaches far into the interior. Formosa, the Ryukyu Islands, and Japan proper for many years before the war were kept relatively free of cholera, although the tendency for it to reach these islands from China is great. Very few, if any, cases of cholera have ever been reported from the Japanese Mandated Islands or Guam. In the years 1930-34 an extensive epidemic occurred in many parts of the Far East, reaching as far north as Peiping, China. Cholera was also widespread in 1938-39. The great epidemics of the nineteenth century reached all but the coldest parts of the world. The potential distribution of cholera, therefore, is nearly universal. In all parts of the Far East especially, the danger of epidemics is ever present.

3. COURSE. *a. Symptoms and signs.* The incubation period is usually from 1 to 3 days. Premonitory symptoms of depression, lack of energy, and simple diarrhea sometimes occur. In epidemics, mild cases may be seen which show

only malaise and diarrhea throughout. In ordinary cases, the onset is sudden, with profuse, watery stools which quickly lose all fecal characteristics. The stools are voluminous and frequent; they are of a light grayish color and contain small mucous flocculi. Tenesmus is uncommon. Vomiting, which is copious, is often precipitate and free of nausea and retching. Prostration rapidly becomes severe. Dehydration may reach an extreme degree in a very short time, so that it is obvious in the thickening of the blood (the specific gravity may rise nearly to 1.070) and in the shrinking of all the tissues. There is great thirst. Patients are apathetic but clear in mind. In addition to huge quantities of fluids, large amounts of mineral metabolites are lost, especially chlorine, sodium, and calcium. There is a strong tendency toward acidosis, and a marked shift may occur in the acid-base balance of the blood (pH as low as 7.07 and bicarbonate reserve as low as 18 vols. per 100 cc, with total base reduced by 10 percent, have been reported). Muscular cramps may be widespread and severe. The circulation is profoundly affected, with peripheral collapse and low blood pressure rapidly developing to marked degree. The secretion of urine often fails and uremia often appears in severe cases. The skin temperature may be subnormal, though the rectal temperature remains elevated. In severe cases, the rectal temperature also falls. In some instances, a stage of "reaction" develops, with high temperature and the appearance of complications, such as pneumonia.

b. Duration and outcome. The course is usually run in a few days (average, 3 to 5). In fatal cases, death may occur in a few hours or after several days. Even in recent years, epidemics among neglected patients show a fatality rate of 50 to 70 percent. When proper treatment is promptly applied, the case fatality rate should not be over 8 to 10 percent.

4. DIAGNOSIS. *a. General.* The possibility of cholera should be brought to mind by epidemiologic considerations. In and near endemic areas, it is essential to be informed of cases suspected of being cholera among native populations. The recognition of the first few cases of cholera in an area is a matter of vital importance. At the start of an epidemic, rela-

tively mild ambulatory cases which are exceedingly dangerous as potential source of spread may be mistakenly diagnosed as food poisoning or dysentery. In the presence of an epidemic, every person having diarrhea or gastrointestinal disturbance should be regarded as a cholera suspect until proved otherwise. Cholera must be separated from: acute bacillary dysentery, in which the stool content is different and tenesmus is present (except in mild cases), and in which collapse is rare in adults; food poisoning, in which distressing vomiting with nausea and retching, and headache are common; clinical forms of malaria (chiefly falciparum malaria), in which intestinal symptoms and collapse occur; heat exhaustion and other conditions in which a state of shock develops.

b. Specific. (1) Cholera is diagnosed specifically by the identification of *Vibrio comma* in stool cultures. Fecal smears stained with carbolfuchsin diluted 1 to 10, showing the comma forms with the "fish in stream" appearance, are suggestive. The final diagnosis, however, requires culture of the organism from stool specimens and identification by agglutination.

(2) Specimens of feces from cases or suspected carriers should be planted (two or more loopfuls of liquid feces or mucus) without delay in several tubes of alkaline (pH 8.0 to 8.4) peptone water (peptone 1 percent, NaCl 0.5 percent) and incubated at 37° C. for 6 to 8 hours. Other intestinal organisms are inhibited somewhat at this alkalinity, and the vibrio if present will become concentrated at the surface. Examine the surface growth microscopically for typical gram-negative, slightly curved, motile rods. Streak onto nutrient or infusion agar. Typical 24-hour colonies resemble those of the other enteric gram-negative bacilli. Suspected colonies may be tested with specific *V. comma* agglutinating serum using a slide technique and a 1:20 antiserum dilution.

(3) Colonies giving a positive slide agglutination should be isolated and their identity confirmed by macroscopic tube agglutination and biochemical studies. *V. comma* produces acid without gas in glucose, maltose, mannite, and sucrose. Lactose may become acid in 14 days. Nitrites are produced from nitrates; indol is positive and gelatin is liquefied. Macroscopic tube agglutinations should be done at 37° C. for

2 hours rather than at 56° C., since rapid lysis of the vibrio occurs at the higher temperature. It should be noted that *V. comma* is sometimes strongly or completely inhibited on the selective media such as EMB agar or SS agar used for the isolation of other enteric pathogens.

(4) To isolate the cholera vibrio from suspected water, 100 cc samples are inoculated into 10 cc of 10 percent peptone water and incubated for 6 to 12 hours at 37° C. The surface growth is examined as outlined in (2) above.

5. TREATMENT. *a. General.* A patient with cholera represents a therapeutic emergency. The prompt institution and intelligent management of therapy are essential. Since it usually happens that a group of patients (often a very large number) must be treated at the same time, some general plan of action should be prepared and adhered to unless cogent reasons for deviations appear. An outline of the essential part of the treatment is given in *f* below. As in all severe infections, good general medical and nursing care are important. Patients with subnormal temperatures should be kept warm. During the early stages of the disease, little or no attempt should be made to give the patient food, except such as he may be able to take in liquid form.

b. Isolation. See paragraph 6a.

c. Replacement of fluids and electrolytes. At present this is without doubt the most important form of treatment, far outranking any available drug or serum therapy. Those who are familiar with the urgency of this form of treatment in young children with dysentery will recognize the similarity of the situations. However, even in moderately severe cases of cholera the problem is much more difficult and persistent. During the acute stage, patients usually can retain only very little of the fluid taken by mouth (advantage should be taken, however, of any possibility that they can retain fluid taken by this route). Reliance must be placed, therefore, upon intravenous injections. Subcutaneous injections are not recommended.

d. Types of solutions. If sufficient supplies of standard solutions and standard sterile distilled water for intravenous administration are not available, solutions should be freshly prepared with distilled water and freshly sterilized. Many "reactions" described in cholera

are due to pyrogenic impurities in water. However, in grave emergencies when large groups of patients must be treated, the administration of fluid should not be withheld because of inability to use ideal technique. Plasma and whole blood generally are not necessary in cholera and *may be very harmful*. The state of shock which accompanies cholera is not in itself an indication for plasma. Plasma and blood should be given only when specific reasons for giving them are known to exist. The three solutions described below, with or without dextrose and thiamin, are given intravenously to meet various needs which develop in the course of cholera (see *e* below).

(1) Isotonic saline: sodium chloride 9 gm per liter.

(2) Hypertonic saline: sodium chloride 14 gm per liter. This solution should be prepared by adding sodium chloride (ACS) 14 gm to about 1,100 cc of freshly distilled water and boiling to the point where the volume is 1,000 cc.

(3) Alkaline saline: sodium bicarbonate 18 gm and sodium chloride 6 gm per liter. This solution should not be sterilized by heat because of the attendant loss of carbon dioxide. The following technique may be employed: Dissolve sodium chloride (ACS) 6 gm in about 1,100 cc of freshly distilled water and sterilize by boiling to the point where the volume is 1,000 cc. Add immediately sodium bicarbonate (USP) 18 gm which has been taken directly from the original container and weighed in a sterile vessel. Cool the solution to body temperature and use it at once.

(4) Dextrose to make 5 percent solution should be added to physiologic or hypertonic saline, but not more than 50 gm of glucose should be given in 1 hour or 400 gm in 24 hours. It is desirable, but not essential, to add thiamin chloride 1 mgm for every 25 gm of glucose.

e. Determination of amount, frequency, and type of fluid. (1) The inexperienced physician needs first to learn that patients with cholera usually require relatively huge amounts of fluid and that such treatment may have to be continued over a surprisingly long period. Secondly, he must learn that too much fluid is dangerous, particularly if given after the blood has approached its normal specific gravity. The criterion which has been most used in an

effort to be exact is the specific gravity of the blood which is normally from 1.056 to 1.058. As the normal value is closely approached, the rate of fluid administration should be slowed, but the patient must be watched to see that further large losses of fluid are not occurring and do not begin again. The specific gravity of the blood may be determined by the copper sulfate method (see the *Bulletin of the United States Army Medical Department*, number 71, December 1943, page 66), if circumstances permit. Such determinations are by no means necessary for thoroughly satisfactory treatment of patients. In general, judgment must be based especially on the blood pressure; but color and consistency of the blood, rate of the pulse, and amount of urine are also helpful. The development of palpitation, restlessness, pain in the chest, coughing, or edema indicates that too much fluid has already been given. Most patients should have 2 liters of fluid in the first 2 hours. For some time, more fluid is necessary every 3 to 4 hours. The usual rate of continuous infusions (50 to 60 drops per minute) is quite inadequate. It may be necessary to give as much as 6 to 8 liters in the first 24 hours, although 4 or 5 liters are often sufficient. Intravenous fluid may have to be given well into or through the second 24 hours.

(2) In general, physiological saline is the fluid to be used. In regard to the use of glucose, see *d* (4) above. Some observers believe that hypertonic saline in limited amounts gives better results, especially in early cases (before dehydration is severe). As has been pointed out above, the tendency to acidosis is strong. Most patients have an alkali deficit when they come under treatment, and all may develop this condition later if a favorable response is not secured. Hence, it is advised that treatment begin with a limited amount (500 cc) of alkaline saline solution. The further administration of this solution must depend upon observation of the patient. The rate and depth of respiration are not good guides to the presence of acidosis in the acute stage of cholera, though they may be in the later stages. Ketone bodies are not necessarily present in the urine in acidosis due to cholera. Determination of the pH, the carbon dioxide combining power, or the urea content of the blood would be helpful, but such

studies are often impossible. If measurement of urine volume is possible, it is helpful. Continued lack of urine formation is associated with the development of acidosis. The reaction of the urine may be used, within limits, as a guide to the further need for alkali. In the past, many patients have been overdosed with the result that clinical alkalosis appeared.

f. General routine. The following plan is recommended as an initial procedure: Isolate the patient and make certain that all members of the staff understand the system of isolation and disinfection and the need for continuous close observation of the patient and his treatment. Begin at once to administer fluid by vein and give 2,000 cc in the first 2 hours. Of this amount, 1,500 cc should be physiological saline solution with 75 gm glucose and 3 mgm thiamin hydrochloride. The remainder of this amount of 2,000 cc should consist of 500 cc of alkaline saline solution; if available, it is convenient to give the alkaline solution at the start. This amount of saline solution is almost never sufficient to cover the needs of a patient, although it is often not necessary to supply more alkaline solution. Further physiological saline solution, often in the amount of 1,000 cc, will be needed every 3 or 4 hours in many cases. The amount and type of such fluid must be determined in accordance with the principles outlined in *e* above.

g. Chemotherapy. Under no circumstances should the prompt institution of parenteral treatment with liberal amounts of fluid be neglected because of the use of chemotherapy. The value of the sulfonamides and penicillin in the treatment of cholera is uncertain. Because of the frequent failure of renal secretion, it is believed that sulfadiazine and other well absorbed sulfonamides should not be given by any route. Reports of the results of giving sulfaguanidine are difficult to evaluate. The use of sulfaguanidine is suggested; if it is given, full doses should be administered: 5 gm four times a day or 3.5 gm six times a day for 4 or 5 days. The clinical value of penicillin has not been determined. Although the vibrio is gram-negative, the drug has been shown to exert an effect *in vitro*. Penicillin in large dosage therefore should be tried in a suitable series of patients, with adequate controls. Full accounts

of the results of chemotherapy in cholera are desired.

h. Various drugs. Numerous drugs of a great variety have been used in the past, most of which rest on no rational basis and have not been shown to be efficacious. Their use is considered to interfere with the proper treatment of the patient, especially during the acute stage. Included in this group are digitalis, epinephrin, hypnotics, sedatives, and laxatives. In some cases with collapse, the injection of caffeine sodium benzoate may be helpful.

i. Special forms of treatment. No bactericidal or antitoxic serum which is known to be efficacious is available. Claims have been advanced for cholera bacteriophage, but clear evidence of its value is lacking. Its use is not recommended.

j. Convalescence. Once convalescence is established, it usually proceeds rapidly. Patients should be allowed to resume normal activity only gradually. Suitable restrictions must be imposed for the first 2 weeks. The diet should soon be liberal. Most patients can be expected to return to duty in about 30 days.

6. PREVENTION. *a. Isolation.* Patients and proved carriers should be strictly isolated. Special care must be taken in the disposal of excreta and vomitus and all articles which are contaminated by them. Patients' clothing, bedding, and eating utensils should be disinfected by boiling. All attendants should soak their hands in an antiseptic solution and wash them with soap and water *immediately* after handling patients or any article contaminated by them. A cholera ward should be screened and remote from any general source of water and from any mess or kitchen.

b. Foreign quarantine. Cholera is a quarantinable disease as defined in international sanitary codes. Military personnel found or suspected to be infected with cholera are subject to the provisions of such international sanitary regulations except, of course, as their application may be modified by martial law or by the necessity of the military situation. Traditional practice provides for detention of cases and suspects traveling internationally by boat or aircraft until the individual is determined to be uninfected. Decisions are ordinarily based upon physical inspection, evaluation of contact

history, epidemiology of the disease in areas departed, and stool examinations when indicated. Freedom of the stool from cholera vibrios is usually required for release from detention. U. S. Army policy considers that effective immunizations, conditions of sanitation in military carriers and stations, and the constant medical surveillance maintained over personnel traveling in military traffic are adequate guarantees, and that evidence of valid immunization and freedom from symptoms of cholera at the time of travel may be taken to fulfill quarantine requirements without further ado, in order to avoid delay en route.

c. Immunizations. (1) Although cholera vaccination is of proved value, reliance must not be placed upon vaccination as the sole means of preventing cholera. Vaccination is definitely secondary in value to sanitary measures for protection of water and food. These measures must be applied vigorously, even though all personnel are immunized against cholera.

(2) Cholera vaccination is required for personnel stationed in or traveling to or through Asia, including the area around the Persian Gulf, the Philippines, the islands of the East Indies and far western Pacific. It may be required in other areas at the direction of The Surgeon General, or at the discretion of the local surgeon when danger from cholera exists. Initial vaccinations consists of two subcutaneous injections of cholera vaccine at a 7- to 10-day interval. The first dose is 0.5 cc and the second dose 1.0 cc; stimulating doses of 1.0 cc should be administered every 4 to 6 months during danger of infection. Additional doses of 1.0 cc each will be given whenever in the opinion of the surgeon stimulation of immunity is indicated (see par. 4g, TB MED 114).

d. Water supply. When the danger of cholera exists, particular care should be exercised to safeguard water supplies. In the case of fixed installations, a special sanitary survey of the water system should be made by a qualified sanitary engineer, as provided in paragraph 11a(3), AR 40-205, unless such a survey has been made within 6 months previously. A chlorine residual of not less than four-tenths part per million (0.4 ppm) will be maintained in the active part of the distribution system at all times, and daily or more frequent tests of

the residual will be made. In the case of field supplies, water will be checked to insure maintenance of required chlorine residuals until consumed. Drinking water that, due to its organic or mineral content, can not be effectively chlorinated should be boiled and then chlorinated to protect from subsequent contamination. Whenever possible, water should be coagulated, settled, and filtered prior to use, either in fixed filter plants or by portable or mobile purification units. All personnel should be specifically directed not to consume water except from sources approved by the surgeon.

e. Food and food handlers. Food should be eaten only in authorized places, and other establishments should be declared "out of bounds." Native help should be excluded as food handlers at military installations. Personal hygiene, especially the proper cleansing of hands, should be rigidly enforced for all personnel handling food. Fresh fruits and vegetables must be cooked before being eaten, or else soaked for 30 minutes in a concentrated solution of Compound Germicidal Rinse (1 unit dissolved in 8 gallons of water). Compound Germicidal Rinse is QM Stock No. 51-C-1606. Stool cultures on all food handlers should be made at regular intervals. The importance of reporting any symptoms or signs of an intestinal upset, even one loose stool, should be impressed on all food handlers. Individuals known to have been infected should not be permitted to handle food for a period of 3 months after return to duty and then only after three negative stool cultures have been obtained. Careful attention should be paid to the washing and disinfection of eating and cooking utensils, in accordance with AR 40-205 and changes thereto. If boiling water is not available for disinfection, then after washing and rinsing, the dishes and cooking utensils should be immersed in a solution of Compound Germicidal Rinse (1 unit in 25 gallons of water) for a period of at least 1 minute. After cleansing, dishes and cooking utensils should be air dried. During the drying and storage periods they should be protected from insects and dust.

f. Fly control. The control of flies is especially important in areas where cholera is present. Adequate screening of kitchens, messes, isolation wards, and latrines should be

provided and maintained in good repair. Proper disposal of organic waste materials should be enforced to prevent breeding of flies. In the field it is essential that flies be denied access to human feces by flyproof construction of latrines. When native labor is employed, proper latrine facilities should be provided and their use enforced. Destruction of adult flies by the use of insecticides, traps, and swatting should receive close attention, especially in sick wards, kitchens, mess halls, and latrines. DDT may be used to kill adult flies by applying as a residual spray and to kill fly larvae in organic wastes by applying as a spray or powder. Residual spray (5 percent DDT in kerosene, QM Stock No. 51-I-305) applied to surfaces on which flies commonly rest will remain lethal to

[AG 300.5 (31 Jan 45)]

BY ORDER OF THE SECRETARY OF WAR:

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For explanation of symbols, see FM 21-6.